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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:06:28 ON 08 NOV 2001

=> fil .bec
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS,
       ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 11:06:43 ON 08 NOV 2001
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

11 FILES IN THE FILE LIST

=> s deoxynucleoside(4a)kinase#
FILE 'MEDLINE'
           893 DEOXYNUCLEOSIDE
        163592 KINASE#
L1          65 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'SCISEARCH'
           781 DEOXYNUCLEOSIDE
        180295 KINASE#
L2          49 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'LIFESCI'
           416 DEOXYNUCLEOSIDE
         53750 KINASE#
L3          18 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'BIOTECHDS'
           110 DEOXYNUCLEOSIDE
          4670 KINASE#
L4             1 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'BIOSIS'
          1042 DEOXYNUCLEOSIDE
        209827 KINASE#
L5          67 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'EMBASE'
           907 DEOXYNUCLEOSIDE
        140113 KINASE#
L6          52 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'HCAPLUS'
          2003 DEOXYNUCLEOSIDE
        168161 KINASE#
L7         106 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'NTIS'
            11 DEOXYNUCLEOSIDE
          1115 KINASE#
L8             0 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'ESBIOBASE'
           223 DEOXYNUCLEOSIDE
         67435 KINASE#
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L9          16 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'BIOTECHNO'
           435 DEOXYNUCLEOSIDE
         71483 KINASE#
L10         25 DEOXYNUCLEOSIDE(4A)KINASE#

FILE 'WPIDS'
           147 DEOXYNUCLEOSIDE
          4713 KINASE#
L11           3 DEOXYNUCLEOSIDE(4A)KINASE#

TOTAL FOR ALL FILES
L12         402 DEOXYNUCLEOSIDE(4A) KINASE#

=> s l12(10a)(insect or drosophil?)
FILE 'MEDLINE'
         37615 INSECT
         37763 DROSOPHIL?
L13           3 L1 (10A)(INSECT OR DROSOPHIL?)

FILE 'SCISEARCH'
         36081 INSECT
         52070 DROSOPHIL?
L14           3 L2 (10A)(INSECT OR DROSOPHIL?)

FILE 'LIFESCI'
         26229 INSECT
         22792 DROSOPHIL?
L15           1 L3 (10A)(INSECT OR DROSOPHIL?)

FILE 'BIOTECHDS'
          5911 INSECT
           603 DROSOPHIL?
L16           0 L4 (10A)(INSECT OR DROSOPHIL?)

FILE 'BIOSIS'
         71049 INSECT
         56106 DROSOPHIL?
L17           3 L5 (10A)(INSECT OR DROSOPHIL?)

FILE 'EMBASE'
         20448 INSECT
         28340 DROSOPHIL?
L18           3 L6 (10A)(INSECT OR DROSOPHIL?)

FILE 'HCAPLUS'
         54124 INSECT
         34878 DROSOPHIL?
L19           5 L7 (10A)(INSECT OR DROSOPHIL?)

FILE 'NTIS'
          3510 INSECT
           451 DROSOPHIL?
L20           0 L8 (10A)(INSECT OR DROSOPHIL?)

FILE 'ESBIOBASE'
         15182 INSECT
         14536 DROSOPHIL?
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L21           2 L9 (10A)(INSECT OR DROSOPHIL?)

FILE 'BIOTECHNO'
         10483 INSECT
         18065 DROSOPHIL?
L22           2 L10(10A)(INSECT OR DROSOPHIL?)

FILE 'WPIDS'
         26635 INSECT
           372 DROSOPHIL?
L23           1 L11(10A)(INSECT OR DROSOPHIL?)

TOTAL FOR ALL FILES
L24          23 L12(10A)(INSECT OR DROSOPHIL?)

=> s l12 and multifunct?
FILE 'MEDLINE'
          5280 MULTIFUNCT?
L25           4 L1 AND MULTIFUNCT?

FILE 'SCISEARCH'
          8076 MULTIFUNCT?
L26           5 L2 AND MULTIFUNCT?

FILE 'LIFESCI'
          2259 MULTIFUNCT?
L27           1 L3 AND MULTIFUNCT?

FILE 'BIOTECHDS'
           253 MULTIFUNCT?
L28           0 L4 AND MULTIFUNCT?

FILE 'BIOSIS'
          5304 MULTIFUNCT?
L29           4 L5 AND MULTIFUNCT?

FILE 'EMBASE'
          4713 MULTIFUNCT?
L30           4 L6 AND MULTIFUNCT?

FILE 'HCAPLUS'
         12830 MULTIFUNCT?
L31           6 L7 AND MULTIFUNCT?

FILE 'NTIS'
           795 MULTIFUNCT?
L32           0 L8 AND MULTIFUNCT?

FILE 'ESBIOBASE'
          2643 MULTIFUNCT?
L33           2 L9 AND MULTIFUNCT?

FILE 'BIOTECHNO'
          2760 MULTIFUNCT?
L34           3 L10 AND MULTIFUNCT?

FILE 'WPIDS'
          9479 MULTIFUNCT?
L35           0 L11 AND MULTIFUNCT?
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TOTAL FOR ALL FILES
L36          29 L12 AND MULTIFUNCT?

=> s (l24 or l36) not 2000-2001/py
FILE 'MEDLINE'
        823482 2000-2001/PY
L37           3 (L13 OR L25) NOT 2000-2001/PY

FILE 'SCISEARCH'
       1712056 2000-2001/PY
L38           4 (L14 OR L26) NOT 2000-2001/PY

FILE 'LIFESCI'
        144633 2000-2001/PY
L39           1 (L15 OR L27) NOT 2000-2001/PY

FILE 'BIOTECHDS'
         23488 2000-2001/PY
L40           0 (L16 OR L28) NOT 2000-2001/PY

FILE 'BIOSIS'
        896672 2000-2001/PY
L41           3 (L17 OR L29) NOT 2000-2001/PY

FILE 'EMBASE'
        765725 2000-2001/PY
L42           3 (L18 OR L30) NOT 2000-2001/PY

FILE 'HCAPLUS'
       1694037 2000-2001/PY
L43           4 (L19 OR L31) NOT 2000-2001/PY

FILE 'NTIS'
              0 2000-2001/PY
L44           0 (L20 OR L32) NOT 2000-2001/PY

FILE 'ESBIOBASE'
        498328 2000-2001/PY
L45           1 (L21 OR L33) NOT 2000-2001/PY

FILE 'BIOTECHNO'
        209444 2000-2001/PY
L46           2 (L22 OR L34) NOT 2000-2001/PY

FILE 'WPIDS'
       1505844 2000-2001/PY
L47           0 (L23 OR L35) NOT 2000-2001/PY

TOTAL FOR ALL FILES
L48          21 (L24 OR L36) NOT 2000-2001/PY

=> dup rem l48
PROCESSING COMPLETED FOR L48
L49           7 DUP REM L48 (14 DUPLICATES REMOVED)

=> d tot

L49  ANSWER 1 OF 7  BIOSIS  COPYRIGHT 2001 BIOSIS
```

TI The single **deoxynucleoside kinase** in **Drosophila** melanogaster, Dm-dNK, is **multifunctional** and differs from the mammalian **deoxynucleoside kinases.**
SO Griesmacher, A. [Editor]; Chiba, P. [Editor]; Mueller, M. M. [Editor]. Advances in Experimental Medicine and Biology, (1998) Vol. 431, pp. 465-469. Advances in Experimental Medicine and Biology; Purine and pyrimidine metabolism in man IX.
Publisher: Plenum Press 233 Spring Street, New York, New York, USA.
Meeting Info.: Joint IXth International and 6th European Symposium on Purine and Pyrimidine Metabolism in Man Gmunden, Austria June 1-7, 1997
ISSN: 0065-2598. ISBN: 0-306-45778-4.
AU Munch-Petersen, Birgitte (1); Piskur, Jure; Sondergaard, Leif
AN 1999:174433 BIOSIS

L49 ANSWER 2 OF 7 MEDLINE DUPLICATE 1
TI Four **deoxynucleoside kinase** activities from **Drosophila** melanogaster are contained within a single monomeric enzyme, a new **multifunctional deoxynucleoside kinase.**
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Feb 13) 273 (7) 3926-31.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
AU Munch-Petersen B; Piskur J; Sondergaard L
AN 1998129796 MEDLINE

L49 ANSWER 3 OF 7 MEDLINE DUPLICATE 2
TI The single **deoxynucleoside kinase** in **Drosophila** melanogaster, Dm-dNK, is **multifunctional** and differs from the mammalian **deoxynucleoside kinases.**
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 431 465-9.
Journal code: 2LU; 0121103. ISSN: 0065-2598.
AU Munch-Petersen B; Piskur J; Sondergaard L
AN 1998260474 MEDLINE

L49 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2001 ACS
TI **Multifunctional** enzymes for the synthesis of 2'-deoxynucleoside triphosphates and their incorporation in DNA
SO Stud. Org. Chem. (Amsterdam) (1998), 53(New Frontiers in Screening for Microbial Biocatalysts), 247-258
CODEN: SOCHDQ; ISSN: 0165-3253
AU Havlina, Roxana; Cech, Birgit; Holland, Rudi
AN 1998:311703 HCAPLUS
DN 129:109304

L49 ANSWER 5 OF 7 MEDLINE DUPLICATE 3
TI Multisubstrate analogs for **deoxynucleoside kinases.** Triphosphate end products and synthetic bisubstrate analogs exhibit identical modes of binding and are useful probes for distinguishing kinetic mechanisms.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1986 Dec 5) 261 (34) 15836-43.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
AU Ikeda S; Chakravarty R; Ives D H
AN 87057232 MEDLINE

L49 ANSWER 6 OF 7 SCISEARCH COPYRIGHT 2001 ISI (R)
TI **MULTIFUNCTIONAL** BACTERIAL **DEOXYNUCLEOSIDE KINASE** ISOLATED BY BLUE SEPHAROSE CL-6B AFFINITY CHROMATOGRAPHY
SO FEDERATION PROCEEDINGS, (1977) Vol. 36, No. 3, pp. 857.
AU DEIBEL M R (Reprint); IVES D H
AN 77:95521 SCISEARCH

L49 ANSWER 7 OF 7 SCISEARCH COPYRIGHT 2001 ISI (R)
TI BACTERIAL **DEOXYNUCLEOSIDE KINASE** - ALLOSTERIC, **MULTIFUNCTIONAL** ENZYME
SO ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (1975) Vol. 170, pp. 179.
AU DEIBEL M R (Reprint); REZNIK R B; IVES D H
AN 75:306046 SCISEARCH

=> d ab tot

L49 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS

L49 ANSWER 2 OF 7 MEDLINE DUPLICATE 1
AB In mammalian cells, there are three pyrimidine nucleoside salvage enzymes with the capacity to phosphorylate all four deoxynucleosides, the two thymidine kinase isoenzymes, TK1 and TK2, and the deoxycytidine kinase, dCK. TK1 is cell cycle-regulated; TK2 is expressed constitutively and can phosphorylate deoxycytidine to the same extent as thymidine. dCK phosphorylates deoxycytidine, deoxyadenosine, and deoxyguanosine, but not thymidine. In addition, the three kinases can phosphorylate a number of medically important analogs. In cultured **Drosophila** melanogaster embryonic cells, only one pyrimidine **deoxynucleoside kinase** was present. This **kinase** was purified and showed a broad substrate specificity, since it was able to phosphorylate all four deoxynucleosides with high efficiency, as compared with the kinases in mammalian cells. Additionally, a number of nucleoside analogs such as arabinofuranosyl pyrimidines, deoxyuridine, and 5'-fluorodeoxyuridine, were phosphorylated. There was negligible 3'-azidothymidine and no dTMP phosphorylation. The enzyme was active as a monomer of about 30 kDa. We suggest the name D. melanogaster **deoxynucleoside kinase** for this **multifunctional kinase**. The substrate specificity, size, and other characteristics show that this enzyme is more related to human TK2 than to the other mammalian deoxyribonucleoside kinases, but is unique with respect to the capacity to phosphorylate all four deoxynucleosides.

L49 ANSWER 3 OF 7 MEDLINE DUPLICATE 2

L49 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AB During the process of purifying the two known nucleoside ribosyltransferase activities from Lactobacillus leichmannii, a third isoenzyme was assayed as transglycosidation catalyst. It was demonstrated that these three enzymes have not only ribosyltransferase, but also **deoxynucleoside kinase**, ribonucleoside triphosphate reductase, adenosine deaminase and DNA polymerase activity. Some activities show a lag phase (no reaction takes place in the first hours), which is a typical behavior of **multifunctional** enzymes and is ascribed to conformational changes: hysteresis or time cooperativity or kinetic cooperativity.

L49 ANSWER 5 OF 7 MEDLINE DUPLICATE 3
AB Comparative inhibition kinetics with natural dNTP end products (dNp3) and new synthetic bisubstrate-type analogs, dNp4A (deoxynucleoside 5'-adenosine 5'''-P1,P4-tetraphosphate), have been studied with their target **deoxynucleoside kinases** from Lactobacillus acidophilus. Analysis of inhibition specificity, inhibition patterns, and Ki(app) under various conditions has revealed the following conclusions.

Both dNTP and dNp4A bind to the active site of the corresponding kinase through multiple binding determinants. The deoxynucleoside moiety of dNTP fits optimally at the deoxynucleoside binding site and provides the basis for its inhibition specificity, whereas the triphosphate group interacts with the ATP binding site, reinforcing the affinity of the molecule as a potent end product inhibitor (Ki = 0.4-3 microM). The adenosine moiety of dNp4A does not contribute to the binding of this compound, whereas the tetraphosphate portion is the second binding determinant, just as in the model developed for dNTP. dNTP and dNp4A proved to be useful tools for distinguishing the kinetic mechanisms of kinases which follow sequential pathways, i.e. the rapid equilibrium Random Bi Bi for dCyd and dGuo kinases and the steady state Ordered Bi Bi mechanism for two dAdo kinases associated either with dCyd kinase or with dGuo kinase on different **multifunctional** proteins.

L49 ANSWER 6 OF 7 SCISEARCH COPYRIGHT 2001 ISI (R)

L49 ANSWER 7 OF 7 SCISEARCH COPYRIGHT 2001 ISI (R)

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	75.44	75.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.59	-0.59

STN INTERNATIONAL LOGOFF AT 11:24:31 ON 08 NOV 2001

Connection closed by remote host

L Number	Hits	Search Text	DB	Time stamp
1	9	deoxynucleoside near3 kinase$1	USPAT; US-PGPUB	2001/11/08 10:52

US-CL-CURRENT: 435/91.2

US-PAT-NO: 6258568
DOCUMENT-IDENTIFIER: US 6258568 B1
TITLE: Method of sequencing DNA based on the detection of the release of pyrophosphate and enzymatic nucleotide degradation
DATE-ISSUED: July 10, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nyren; Pal	Skarpnack	N/A	N/A	SEX

US-CL-CURRENT: 435/91.1,435/91.2
ABSTRACT:

The present invention relates to a method of sequencing DNA, based on the detection of base incorporation by the release of pyrophosphate (PPi) and simultaneous enzymatic nucleotide degradation.

17 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

DEPR:
In the next series of experiments two different synthetic templates as well as a PCR product were sequenced in order to investigate the feasibility of the new
approach. FIGS. 3 and 4 show the result from DNA sequencing performed on two different synthetic templates. Both templates were sequenced to the end, and in both cases the true sequence could be determined. When the polymerase reaches the end of the template, the signal strongly decreases indicating slower polymerization for the last bases. The signal was not decreased to the same extent if a longer template was sequenced (FIG. 5). The small signals observed when non-complementary bases were added are due to PPi contamination in the nucleotide solutions. The later increase of this background signal (false signals) is probably due to nucleoside diphosphate kinase activity (contamination in the ATP sulfurylase preparation from Sigma). The nucleoside diphosphate kinase converts non-degraded deoxynucleoside diphosphates to deoxynucleoside triphosphates when a new deoxynucleotide triphosphate is added.
The formed deoxynucleoside triphosphate can then be incorporated into the growing primer. This effect was especially obvious when the synthetic template
E3PN as sequenced. When the first correct nucleotide (dCTP) is added some of the non-degraded dTDP is converted to dTTP. After dCMP has been incorporated some of the formed dTTP can be incorporated. This out-of-phase obtained DNA can be further extended when dGTP is added. This is clearly shown when the out-of-phase DNA has reached the position where two A should be incorporated. The false signal is now stronger. The following double T and C also give stronger signals whereas the next single A gives a lower signal. In FIG. 5, DNA sequencing of 20 bases of a 160-base-long self-primed single-stranded PCR product is shown. The obtained sequence was confirmed by semiautomatic solid-phase Sanger sequencing (data not shown). The main reason for the sequencing to come out of phase is a combination of slow degration of deoxynucleoside diphosphates (at least some of the dNDPs) by the potato apyrase
(Liebecq, C. Lallemand A, and Deguldre-Guillaume, M. J. (1963) Bull. Soc. Chim. Biol. 45, 573-594) and the **deoxynucleoside diphosphate kinase** contamination in the ATP sulfurylase preparation obtained from Sigma. It is possible to overcome this problem by using a pure preparation of ATP

sulfurylase, or by using more efficient dNDP degrading enzymes (Doremus, H. D. and Blevins, D. G. (1988) Plant Physiol. 87(1), 41-45). Even if a pure preparation of ATP sulfurylase is used it could be an advantage to use combinations of nucleotide degrading enzymes (NTPase, NDPase, NMPase) to increase the rate of the degradation process and to decrease the thermodynamic equilibrium concentration of dNTPs. In addition, it could be an advantage to use an enzyme with low Km for dNTPs such as the Pig Pancreas nucleoside triphosphate diphosphohydrolase (Le Bel, D., Piriet, G. G. Phaneuf, S., St-Jean, P., Laliberte, J. F. and Beudoin, A. R. (1980) J. Biol. Chem. 255, 1227-1233; Laliberte, J. F. St-Jean, P. and Beudoin, R. (1982) J. Biol Chem. 257, 3869-3871).

US-CL-CURRENT: 378/71,378/73 ,378/79 ,530/364 ,530/388.21 ,536/23.1

US-PAT-NO: 6183121
DOCUMENT-IDENTIFIER: US 6183121 B1
TITLE: Hepatitis C virus helicase crystals and coordinates that define helicase binding pockets
DATE-ISSUED: February 6, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kim; Joseph L.	Natick	MA	N/A	N/A
Morgenstern; Kurt A.	Derry	NH	N/A	N/A
Caron; Paul R.	Malden	MA	N/A	N/A
Lin; Chao	Brookline	MA	N/A	N/A

ABSTRACT:
The invention relates to the X-ray crystal structure of the hepatitis C virus helicase domain. More specifically, the invention relates to crystallized complexes of HCV helicase and an oligonucleotide, to crystallizable compositions of HCV helicase and an oligonucleotide and to methods of crystallizing an HCV helicase-oligonucleotide complex. The invention further relates to a computer programmed with the structure coordinates of the HCV helicase oligonucleotide binding pocket or the HCV helicase nucleotide triphosphate pocket wherein said computer is capable of displaying a three-dimensional representation of that binding pocket.
17 Claims, 86 Drawing figures
Exemplary Claim Number: 8
Number of Drawing Sheets: 84

DRPR:
FIG. 7A depicts the residues surrounding the bound sulfate superimposed on the phosphate binding loops of eight **deoxynucleoside monophosphate kinases**.

US-CL-CURRENT: 435/85,435/87 ,435/88 ,435/91.1 ,435/91.5

US-PAT-NO: 6087132
DOCUMENT-IDENTIFIER: US 6087132 A
TITLE: Multi-functional enzymes including derivable 2'3'-dideoxyribofuranoside triprosphates
DATE-ISSUED: July 11, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vasiloiu; Roxana	Frankfurt M. 60	N/A	N/A	DEX

US-CL-CURRENT: 435/89,435/85 ,435/87 ,435/88 ,435/91.1 ,435/91.5

ABSTRACT:
The invention relates to a multifunctional nucleoside didesoxyribosyl or nucleoside deoxyribosyl transferase which has one or more of the following additional activities (desoxy) nucleoside kinase, nucleoside reductase desaminase, or DNA polymerase activity. Utilizing the multifunctional enzyme results in a variety of nucleic acid products. These products can be prepared using sequential reactions in a single batch process wherein the sequential reaction can be caused to occur by varying process conditions in a manner which
turns on or off the requisite activities causing the sequential reactions to occur. An example of a product prepared in this manner is dideoxyribofuranoside triphosphate. Certain of the resultant products have pharmaceutical activities, e.g. antiviral agents. Lactobacillus leichmannii (DSM 20076) is a source of the multifunctional nucleoside deoxyribosyl transferase.
9 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

BSPR:
This capability has already been noted by J. P. Durham and D. H. Ives, who worked on the **deoxynucleoside kinase** activity of the multifunctional enzymes, but they were unable to identify the end product (1).

US-CL-CURRENT: 435/320.1

US-PAT-NO: 6017896
DOCUMENT-IDENTIFIER: US 6017896 A
TITLE: Purine nucleoside phosphorylase gene therapy for human malignancy
DATE-ISSUED: January 25, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sorscher; Eric J.	Birmingham	AL	N/A	N/A
Bennett, Jr.; Leonard L.	Birmingham	AL	N/A	N/A
Parker; William B.	Birmingham	AL	N/A	N/A

US-CL-CURRENT: 514/44,435/320.1
ABSTRACT:
The present invention provides a method of killing replicating or non-replicating, transfected or transduced mammalian cells and bystander cells, comprising: (a) transfecting or transducing mammalian cells with a nucleic acid encoding a non-human purine cleavage enzyme; and (b) contacting the transfected or transduced cells with an effective amount of a substrate for the purine cleavage enzyme, wherein the substrate is non-toxic to mammalian cells and is cleaved by the enzyme to yield a purine toxic to the targeted mammalian cells and bystander cells, to kill the mammalian cells expressing the enzyme and the bystander cells. Further provided is a vector comprising a DNA sequence coding for a non-human purine nucleoside phosphorylase protein and the vector is capable of replication and/or expression in a host which comprises, in operable linkage: a) optionally, an origin of replication; b) a promoter; and c) a DNA sequence coding for said protein.
12 Claims, 34 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 36

DEPR:
In a preferred embodiment described in the Examples, the substrate is 9-(.beta.-D-2-deoxyerythropentofuranosyl)-6-methylpurine (MeP-dR). Although MeP-dR is relatively non-toxic, the therapeutic index of this compound can be enhanced. For instance, if the toxicity of MeP-dR is due to phosphorylation by a **deoxynucleoside kinase,** then analogs that cannot be phosphorylated, such as 5'-deoxy-MeP-dR, can be synthesized and used as the prodrug to generate MeP in vivo.

US-CL-CURRENT: 435/194,435/252.3 ,435/320.1 ,435/6 ,530/350 ,536/23.1
,536/23.5
,536/24.31 ,536/24.33

US-PAT-NO: 5817482
DOCUMENT-IDENTIFIER: US 5817482 A
TITLE: Disease related nucleotide kinases
DATE-ISSUED: October 6, 1998
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bandman; Olga	Mountain View	CA	N/A	N/A
Hillman; Jennifer L.	Mountain View	CA	N/A	N/A
Hawkins; Phillip R.	Mountain View	CA	N/A	N/A
Guegler; Karl J.	Menlo Park	CA	N/A	N/A
Corley; Neil C.	Mountain View	CA	N/A	N/A

US-CL-CURRENT: 435/69.1,435/194 ,435/252.3 ,435/320.1 ,435/6 ,530/350
,536/23.1
,536/23.5 ,536/24.31 ,536/24.33
ABSTRACT:
The invention provides human nucleotide kinases and polynucleotides which identify and encode DRNK. The invention also provides expression vectors, host
cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders associated with expression of DRNK.
11 Claims, 19 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 19

BSPR:
Nucleoside kinases perform the first step in the nucleotide kinase "cascade" by
phosphorylating various nucleosides. These nucleoside monophosphates become substrates for further phosphorylation to di- and triphosphates. Some nucleoside kinases have a rather broad substrate specificity. Human deoxycytidine kinase (dCK), for example, phosphorylates not only dC, but also dA, dG and various analogs of these natural nucleosides (Chottiner, E. G. et al. (1991) Proc. Natl. Acad. Sci. 88:1531-35). Similarly, deoxyguanosine kinase (dGK) has an overlapping substrate specificity with dCK and its activity
is often indistinguishable from that of the latter enzyme. However, dCK is found at much higher levels in proliferating cells and lymphoid tissues, while dGK is the only **deoxynucleoside kinase** found in non-dividing nerve cells and muscle cells (Wang, L. et al. (1996) FEBS 390:39-43).

US-CL-CURRENT: 424/450,435/252.1 ,435/320.1 ,435/371 ,435/456 ,435/488 ,514/2 ,514/43 ,514/44 ,530/350 ,536/23.2 ,536/23.7 ,536/24.1

US-PAT-NO: 5552311
DOCUMENT-IDENTIFIER: US 5552311 A
TITLE: Purine nucleoside phosphorylase gene therapy for human malignancy
DATE-ISSUED: September 3, 1996
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sorscher; Eric J.	Birmingham	AL	N/A	N/A
Parker; William B.	Birmingham	AL	N/A	N/A
Bennett, Jr.; Leonard L.	Birmingham	AL	N/A	N/A

US-CL-CURRENT: 435/348,424/450 ,435/252.1 ,435/320.1 ,435/371 ,435/456 ,435/488
,514/2 ,514/43 ,514/44 ,530/350 ,536/23.2 ,536/23.7 ,536/24.1
ABSTRACT:
The invention provides a method of killing replicating or non-replicating, transfected or transduced mammalian cells and bystander cells, comprising the following steps: (a) transfecting or transducing mammalian cells with a nucleic
acid encoding a non-human purine nucleoside phosphorylase (PNP); and (b) contacting the transfected or transduced cells with an amount of a substrate for the purine nucleoside phosphorylase sufficient to produce a toxic purine base-analog thereby killing the transfected or transduced cells and bystander cells. In the present method of killing cells, the non-human purine nucleoside
phosphorylase can be an E. coli purine nucleoside phosphorylase. The method of
the invention described above can utilize a substrate that is a purine nucleoside analog. For instance, in the method provided in the Examples, the substrate is 9-(.beta.-D-2-deoxyerythropentofuranosyl)-6-methylpurine (MeP-dR).
14 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

DEPR:
Although MeP-dR is relatively non-toxic, by defining the mechanism of its toxicity, it may be possible to further enhance the therapeutic index of this compound. For instance, if the toxicity of MeP-dR is due to phosphorylation by
a **deoxynucleoside kinase**, then analogs that cannot be phosphorylated, such as 5'-deoxy-MeP-dR, could be synthesized and used as the prodrug to deliver MeP.

US-CL-CURRENT: 424/227.1,435/254.21 ,435/320.1 ,435/483 ,536/24.1

US-PAT-NO: 4803164
DOCUMENT-IDENTIFIER: US 4803164 A
TITLE: Preparation of hepatitis b surface antigen in yeast
DATE-ISSUED: February 7, 1989
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hitzeman; Ronald A.	Pacifica	CA	N/A	N/A
Levinson; Arthur D.	Burlingame	CA	N/A	N/A
Yansura; Daniel G.	San Francisco	CA	N/A	N/A

US-CL-CURRENT: 435/69.3,424/227.1 ,435/254.21 ,435/320.1 ,435/483 ,536/24.1
ABSTRACT:

Hepatitis surface antigen is synthesized in recombinant yeast hosts transformed with vectors encoding hepatitis surface antigen, preferably under the control of the yeast PGK promoter and preferably in the absence of DNA encoding the surface antigen precursor. Hepatitis surface antigen is assembled
by yeast into antigenic 22 nm particles even though hepatitis surface antigen bacterial transformants were not known to be capable of assembling the surface antigen into 22 nm particles.
11 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

DEPR:
Restriction enzymes EcoRI and HindIII along with bacterial alkaline phosphatase
were purchased from Bethesda Research Laboratories. DNA polymerase (Klenow fragment) was purchased for Boehringer-Mannheim. T.sub.4 polynucleotide **kinase, ATP and the deoxynucleoside** triphosphates dATP, dGTP, dCTP and dTTP were purchased from PL Biochemicals. All other DNA restriction and metabolic enzymes were purchased from New England Biolabs. [.gamma.-.sup.32 P]ATP was purchased from Amersham Corp. DNA restriction and metabolic enzymes were used in conditions exactly described by their respective manufacturers.

US-CL-CURRENT: 536/26.8,536/28.5 ,536/28.52

US-PAT-NO: 4788181
DOCUMENT-IDENTIFIER: US 4788181 A
TITLE: 5-substituted-2',3'-dideoxycytidine compounds with anti-HTLV-III activity
DATE-ISSUED: November 29, 1988
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Driscoll; John S.	Rockville	MD	N/A	N/A
Marquez; Victor E.	Gaithersburg	MD	N/A	N/A
Kim; Chong-Ho	Hyattsville	MD	N/A	N/A
Kelley; James A.	Silver Spring	MD	N/A	N/A

US-CL-CURRENT: 514/49,536/26.8 ,536/28.5 ,536/28.52
ABSTRACT:
5-substituted 2',3'-dideoxycytidine compounds and their monophosphates are disclosed which have been found to have potent activity against retroviruses. The 5-fluoro-and 5-aza-substituted 2',3'-dideoycytidine compounds have been found to be effective against HTLV-III/LAV virus.
8 Claims, 0 Drawing figures
Exemplary Claim Number: 7

DEPR:
In order to be active against HTLV-III/LAV reverse transcriptase, the 2',3'-dideoxynucleosides must be converted to their 5'triphosphates. The rate at which these nucleotides are formed appears to vary with the type of cells treated. The first step in this metabolic process, the formation of the monophosphate, is critical, since a high nucleoside K.sub.m value for the appropriate **deoxynucleoside kinase** can result in poor reverse transcriptase inhibitory activity. Additionally, reduced kinase activity can be a cause for the development of resistance as is the case with nucleoside antitumor agents. While it is generally thought that nucleotides do not readily penetrate cell membranes because of their ionic character and relatively low lipophilicity, the nucleoside monophosphates, if effective, would be obviously superior to unphosphorylated drugs. In 1975, Plunkett and Cohen reported, in Cancer Research, 1975, 35, 1547-1554, that 2',3'-dideoxyadenosine-5'-phosphate appeared to enter mouse fibroblasts intact, with cytotoxic consequences.

US-CL-CURRENT: 536/26.23,536/28.5 ,536/28.51

US-PAT-NO: 4471113
DOCUMENT-IDENTIFIER: US 4471113 A
TITLE: Prodrugs based on phospholipid-nucleoside conjugates
DATE-ISSUED: September 11, 1984
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
MacCoss; Malcolm	Naperville	IL	N/A	N/A

US-CL-CURRENT: 536/26.8,536/26.23 ,536/28.5 ,536/28.51

ABSTRACT:
The invention relates to the production of a single diastereomeric form of a phospholipid araC conjugate as a prodrug.
5 Claims, 0 Drawing figures
Exemplary Claim Number: 1,3

BSPR:
There are several problems in chemotherapy with the arabinonucleosides araC and araA. The first is their rapid catabolism via deaminase enzymes to ineffective metabolites. In the case of araC, high levels of deoxycytidine deaminase exist in the liver of humans, and the ineffective metabolite 1-.beta.-D-arabinofuranosyluracial (araU) appears rapidly in human urine after injection of araC. Due to this degradation, the half-life of araC in humans has been estimated to be only 3 to 9 minutes. The second problem is the eventual resistance developed by the cells. In experimental tumor systems, this resistance has been attributed to the selection of cells in which the **deoxynucleoside kinases** have a low specific activity compared to the wild type, so that the arabinoside is not metabolized to the 5'-triphosphate, the actual cytotoxic metabolite. A third problem is the toxicity of the arabinonucleosides in rapidly dividing normal tissue as well as against neoplastic cell types.